

CORRECTED VERSION

(19) World Intellectual Property Organization
International Bureau(43) International Publication Date
13 September 2001 (13.09.2001)

PCT

(10) International Publication Number
WO 01/66155 A2(51) International Patent Classification⁷: **A61K 51/04,**
51/10

(21) International Application Number: PCT/US01/05927

(22) International Filing Date: 23 February 2001 (23.02.2001)

(25) Filing Language: English

(26) Publication Language: English

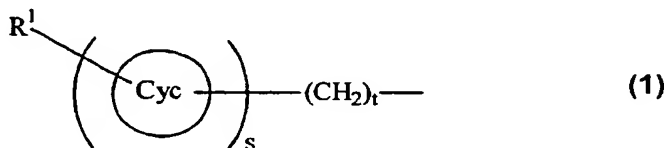
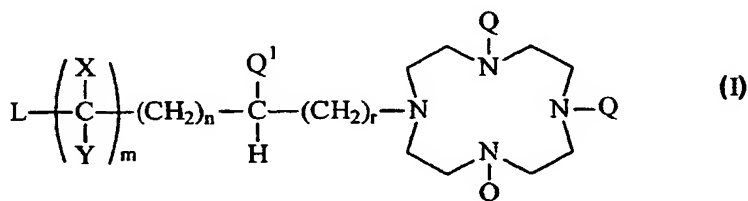
(30) Priority Data:
60/185,220 25 February 2000 (25.02.2000) US

(71) Applicants and

(72) Inventors: **MA, Dangshe** [US/US]: 13011 Twinbrook
Parkway, Rockville, MD 20851 (US). **MCDEVITT,**
Michael, R. [US/US]: Apartment 6A, 5644 Netherland
Avenue, Bronx, NY 10471 (US). **SCHEINBERG, David,**
A. [US/US]: 325 Central Park West, New York, NY10025 (US). **SIMON, Jaime** [US/US]: Route 1, Box
199-A, Angleton, TX 77515 (US). **KIEFER, Garry, E.**
[US/US]: 114 Juniper Street, Lake Jackson, TX 77566
(US). **FRANK, R., Keith** [US/US]: 213 Pansy Path, Lake
Jackson, TX 77566 (US). **GULYAS, Gyongyi** [US/US]:
305 Timbercreek Drive, Lake Jackson, TX 77566 (US).(74) Agent: **KARADZIC, Dragan, J.**: The Dow Chemical
Company, Intellectual Property, B-1211, 2301 N. Bra-
zosport Boulevard, Freeport, TX 77541 (US).(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CZ, DE,
DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
TZ, UA, UG, US, UZ, YU, ZA, ZW.(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian

[Continued on next page]

(54) Title: ACTINIUM-225 COMPLEXES AND CONJUGATES FOR RADIOIMMUNOTHERAPY



(57) **Abstract:** Actinium-225 (²²⁵Ac) complexes with functionalized chelants of the formula (I) wherein: each Q is independently hydrogen or (CHR⁵)_pCO₂R; Q¹ is hydrogen or (CHR⁵)_wCO₂R; each R independently is hydrogen, benzyl or C₁-C₄ alkyl; with the proviso that at least two of the sum of Q and Q¹ must be other than hydrogen; each R⁵ independently is hydrogen; C₁-C₄ alkyl or (C₁-C₂ alkyl)phenyl; X and Y are each independently hydrogen or may be taken with an adjacent X and Y to form an additional carbon-carbon bond; n is 0 or 1; m is an integer from 0 to 10 inclusive; p is 1 or 2; r is 0 or 1; w is 0 or 1; with the proviso that n is only 1 when X and/or Y form an additional carbon to carbon bond, and the sum of r and w is 0 or 1; L is a linker/spacer group covalently bonded to, and replaces one hydrogen atom of one of the carbon atoms to which it is joined, said linker/spacer group being represented by the formula (1) wherein s is an integer of 0 or 1; t is an integer of 0 to 20 inclusive; R¹ is an electrophilic or nucleophilic moiety which allows for covalent attachment to an antibody or fragment thereof, or synthetic linker which can be attached to an antibody or fragment thereof, or precursor thereof; and Cyc represents a cyclic aliphatic moiety, aromatic moiety, aliphatic heterocyclic moiety, or aromatic heterocyclic moiety, each of said moieties optionally substituted with one or more groups which do not interfere with binding to an antibody or antibody fragment; with the proviso that when s, t, m, r, and n are 0, then R¹ is other than carboxyl; their pharmaceutically acceptable salts, their conjugates and the use thereof for radioimmunotherapy is disclosed.



patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

- without international search report and to be republished upon receipt of that report

(48) Date of publication of this corrected version:

7 February 2002

(15) Information about Correction:

see PCT Gazette No. 06/2002 of 7 February 2002, Section II

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
13 September 2001 (13.09.2001)

PCT

(10) International Publication Number
WO 01/66155 A2

(51) International Patent Classification⁷: **A61K 51/04**,
51/10

Jackson, TX 77566 (US). **GULYAS, Gyongyi** [US/US];
305 Timbercreek Drive, Lake Jackson, TX 77566 (US).

(21) International Application Number: PCT/US01/05927

(74) Agent: **KARADZIC, Dragan, J.**; The Dow Chemical
Company, Intellectual Property, B-1211, 2301 N. Bra-
zospport Boulevard, Freeport, TX 77541 (US).

(22) International Filing Date: 23 February 2001 (23.02.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/185,220 25 February 2000 (25.02.2000) US

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CZ, DE,
DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
TZ, UA, UG, US, UZ, YU, ZA, ZW.

(71) Applicant and

(72) Inventor: **MA, Dangshe** [US/US]; 13011 Twinbrook
Parkway, Rockville, MD 20851 (US).

(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian
patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European
patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,
IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **MCDEVITT,**
Michael, R. [US/US]; Apartment 6A, 5644 Netherland
Avenue, Bronx, NY 10471 (US). **SCHEINBERG, David,**
A. [US/US]; 325 Central Park West, New York, NY
10025 (US). **SIMON, Jaime** [US/US]; Route 1, Box
199-A, Angleton, TX 77515 (US). **KIEFER, Garry, E.**
[US/US]; 114 Juniper Street, Lake Jackson, TX 77566
(US). **FRANK, R., Keith** [US/US]; 213 Pansy Path, Lake

Published:

— without international search report and to be republished
upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: ACTINIUM-225 COMPLEXES AND CONJUGATES FOR RADIOIMMUNOTHERAPY

(57) Abstract: Actinium-225 (²²⁵Ac) complexes with functionalized chelants of the formula (I) wherein: each Q is independently hydrogen or (CHR⁵)_nCO₂R; Q¹ is hydrogen or (CHR⁵)_mCO₂R; each R independently is hydrogen, benzyl or C₁-C₄ alkyl; with the proviso that at least two of the sum of Q and Q¹ must be other than hydrogen; each R⁵ independently is hydrogen; C₁-C₄ alkyl or (C₁-C₂ alkyl)phenyl; X and Y are each independently hydrogen or may be taken with an adjacent X and Y to form an additional carbon-carbon bond; n is 0 or 1; m is an integer from 0 to 10 inclusive; p is 1 or 2; r is 0 or 1; w is 0 or 1; with the proviso that n is only 1 when X and/or Y form an additional carbon to carbon bond, and the sum of r and w is 0 or 1; L is a linker/spacer group covalently bonded to, and replaces one hydrogen atom of one of the carbon atoms to which it is joined, said linker/spacer group being represented by the formula (1) wherein s is an integer of 0 or 1; t is an integer of 0 to 20 inclusive; R¹ is an electrophilic or nucleophilic moiety which allows for covalent attachment to an antibody or fragment thereof, or synthetic linker which can be attached to an antibody or fragment thereof, or precursor thereof; and Cyc represents a cyclic aliphatic moiety, aromatic moiety, aliphatic heterocyclic moiety, or aromatic heterocyclic moiety, each of said moieties optionally substituted with one or more groups which do not interfere with binding to an antibody or antibody fragment; with the proviso that when s, t, m, r, and n are 0, then R¹ is other than carboxyl; their pharmaceutically acceptable salts, their conjugates and the use thereof for radioimmunotherapy is disclosed.

WO 01/66155 A2

REPLACED
BY RO/US

HOME COPY

PCT

REQUEST

The undersigned requests that the present
international application be processed
according to the Patent Cooperation Treaty.

1

For receiving Office use only

International Application No.	PCT/US. 01/05927
International Filing Date	(23.02.01) 23 FEB 2001
PCT INTERNATIONAL APPLICATION RO/US	
Name of Receiving Office and "PCT International Application"	
Applicant's or Agent's file reference 60364A	

Box No. I TITLE OF INVENTION ACTINIUM-225 COMPLEXES AND CONJUGATES FOR RADIOIMMUNOTHERAPY	
Box No. II APPLICANT	
Name and address: MA, Dangshe 13011 Twinbrook Parkway Rockville, Maryland 20851 United States of America	<input checked="" type="checkbox"/> This person is also inventor. Telephone No. (979) 238-2845 Facsimile No. (979) 238-0878 Teleprinter No.
State (that is, country) of nationality: US	State (that is, country) of residence: US
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box	
Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)	
Name and address: MCDEVITT, Michael R. 5644 Netherland Avenue Apartment 6A Bronx, New York 10471 United States of America	This person is: <input type="checkbox"/> applicant only <input checked="" type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)
State (that is, country) of nationality: US	State (that is, country) of residence: US
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box	
<input checked="" type="checkbox"/> Further applicants and/or (further) inventors are indicated on a continuation sheet.	
Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE	
The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: <input checked="" type="checkbox"/> agent <input type="checkbox"/> common representative	
Name and address: KARADZIC, Dragan J. The Dow Chemical Company Intellectual Property, B-1211 2301 N. Brazosport Boulevard Freeport, Texas 77541 United States of America	Telephone No. (979) 238-2845 Facsimile No. (979) 238-0878 Teleprinter No.
<input type="checkbox"/> Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.	

Corresponds to: Form PCT/RO/101 (first sheet) (January 2001)

Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)			
If none of the following sub-boxes is used, this sheet is not to be included in the request.			
Name and address: SCHEINBERG, David A. 325 Central Park West New York, New York 10025 United States of America		This person is: <input type="checkbox"/> applicant only <input checked="" type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)	
State (that is, country) of nationality: US		State (that is, country) of residence: US	
This person is applicant for the purposes of:		<input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box	
Name and address: SIMON, Jaime Route 1, Box 199-A Angleton, Texas 77515 United States of America		This person is: <input type="checkbox"/> applicant only <input checked="" type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)	
State (that is, country) of nationality: US		State (that is, country) of residence: US	
This person is applicant for the purposes of:		<input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box	
Name and address: KIEFER, Garry E. 114 Juniper Street Lake Jackson, Texas 77566 United States of America		This person is: <input type="checkbox"/> applicant only <input checked="" type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)	
State (that is, country) of nationality: US		State (that is, country) of residence: US	
This person is applicant for the purposes of:		<input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box	
Name and address: FRANK, R. Keith 213 Pansy Path Lake Jackson, Texas 77566 United States of America		This person is: <input type="checkbox"/> applicant only <input checked="" type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)	
State (that is, country) of nationality: US		State (that is, country) of residence: US	
This person is applicant for the purposes of:		<input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box	
<input checked="" type="checkbox"/> Further applicants and/or (further) inventors are indicated on another continuation sheet			

Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)			
<i>If none of the following sub-boxes is used, this sheet is not to be included in the request.</i>			
Name and address: GULYAS, Gyongyi 305 Timbercreek Drive Lake Jackson, Texas 77566 United States of America		This person is: <input type="checkbox"/> applicant only <input checked="" type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only <i>(If this check-box is marked, do not fill in below.)</i>	
State (that is, country) of nationality: US		State (that is, country) of residence: US	
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box			
Name and address:		This person is: <input type="checkbox"/> applicant only <input type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only <i>(If this check-box is marked, do not fill in below.)</i>	
State (that is, country) of nationality:		State (that is, country) of residence:	
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box			
Name and address:		This person is: <input type="checkbox"/> applicant only <input type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only <i>(If this check-box is marked, do not fill in below.)</i>	
State (that is, country) of nationality:		State (that is, country) of residence:	
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box			
Name and address:		This person is: <input type="checkbox"/> applicant only <input type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only <i>(If this check-box is marked, do not fill in below.)</i>	
State (that is, country) of nationality:		State (that is, country) of residence:	
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box			
<input type="checkbox"/> Further applicants and/or (further) inventors are indicated on another continuation sheet			

Box No. V DESIGNATION OF STATES

The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):

Regional Patent

- ☒ AP ARIPO Patent: GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, MZ Mozambique, SU Sudea, SL Sierra Leone, SZ Swaziland, TZ United Republic of Tanzania, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- ☒ EA Eurasian Patent: AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- ☒ EP European Patent: AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, TR Turkey, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ☒ OA OAPI Patent: BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on line)

National Patent (if other kind of protection or treatment desired, specify on line):

- | | |
|---|--|
| <input checked="" type="checkbox"/> AE United Arab Emirates | <input checked="" type="checkbox"/> LC Saint Lucia |
| <input checked="" type="checkbox"/> AL Albania | <input checked="" type="checkbox"/> LK Sri Lanka |
| <input checked="" type="checkbox"/> AG Antigua & Barbuda | <input checked="" type="checkbox"/> LR Liberia |
| <input checked="" type="checkbox"/> AM Armenia | <input checked="" type="checkbox"/> LS Lesotho |
| <input checked="" type="checkbox"/> AT Austria | <input checked="" type="checkbox"/> LT Lithuania |
| <input checked="" type="checkbox"/> AU Australia | <input checked="" type="checkbox"/> LU Luxembourg |
| <input checked="" type="checkbox"/> AZ Azerbaijan | <input checked="" type="checkbox"/> LV Latvia |
| <input checked="" type="checkbox"/> BA Bosnia and Herzegovina | <input checked="" type="checkbox"/> MA Morocco |
| <input checked="" type="checkbox"/> BB Barbados | <input checked="" type="checkbox"/> MD Republic of Moldova |
| <input checked="" type="checkbox"/> BG Bulgaria | <input checked="" type="checkbox"/> MG Madagascar |
| <input checked="" type="checkbox"/> BR Brazil | <input checked="" type="checkbox"/> MK The former Yugoslav Republic of Macedonia |
| <input checked="" type="checkbox"/> BY Belarus | <input checked="" type="checkbox"/> MN Mongolia |
| <input checked="" type="checkbox"/> BZ Belize | <input checked="" type="checkbox"/> MW Malawi |
| <input checked="" type="checkbox"/> CA Canada | <input checked="" type="checkbox"/> MX Mexico |
| <input checked="" type="checkbox"/> CH and LI Switzerland and Liechtenstein | <input checked="" type="checkbox"/> MZ Mozambique |
| <input checked="" type="checkbox"/> CN China | <input checked="" type="checkbox"/> NO Norway |
| <input checked="" type="checkbox"/> CR Costa Rica | <input checked="" type="checkbox"/> NZ New Zealand |
| <input type="checkbox"/> CU Cuba | <input checked="" type="checkbox"/> PL Poland |
| <input checked="" type="checkbox"/> CZ Czech Republic | <input checked="" type="checkbox"/> PT Portugal |
| <input checked="" type="checkbox"/> DE Germany | <input checked="" type="checkbox"/> RO Romania |
| <input checked="" type="checkbox"/> DK Denmark | <input checked="" type="checkbox"/> RU Russian Federation |
| <input checked="" type="checkbox"/> DM Dominica | <input checked="" type="checkbox"/> SD Sudan |
| <input checked="" type="checkbox"/> DZ Algeria | <input checked="" type="checkbox"/> SE Sweden |
| <input checked="" type="checkbox"/> EE Estonia | <input checked="" type="checkbox"/> SG Singapore |
| <input checked="" type="checkbox"/> ES Spain | <input checked="" type="checkbox"/> SI Slovenia |
| <input checked="" type="checkbox"/> FI Finland | <input checked="" type="checkbox"/> SK Slovakia |
| <input checked="" type="checkbox"/> GB United Kingdom | <input checked="" type="checkbox"/> SL Sierra Leone |
| <input checked="" type="checkbox"/> GD Grenada | <input checked="" type="checkbox"/> TJ Tajikistan |
| <input checked="" type="checkbox"/> GE Georgia | <input checked="" type="checkbox"/> TM Turkmenistan |
| <input checked="" type="checkbox"/> GH Ghana | <input checked="" type="checkbox"/> TR Turkey |
| <input checked="" type="checkbox"/> GM Gambia | <input checked="" type="checkbox"/> TT Trinidad and Tobago |
| <input checked="" type="checkbox"/> HR Croatia | <input checked="" type="checkbox"/> TZ United Republic of Tanzania |
| <input checked="" type="checkbox"/> HU Hungary | <input checked="" type="checkbox"/> UA Ukraine |
| <input checked="" type="checkbox"/> ID Indonesia | <input checked="" type="checkbox"/> UG Uganda |
| <input checked="" type="checkbox"/> IL Israel | <input checked="" type="checkbox"/> US United States of America |
| <input checked="" type="checkbox"/> IN India | <input checked="" type="checkbox"/> UZ Uzbekistan |
| <input checked="" type="checkbox"/> IS Iceland | <input type="checkbox"/> VN Viet Nam |
| <input checked="" type="checkbox"/> JP Japan | <input checked="" type="checkbox"/> YU Yugoslavia |
| <input checked="" type="checkbox"/> KE Kenya | <input checked="" type="checkbox"/> ZA South Africa |
| <input checked="" type="checkbox"/> KG Kyrgyzstan | <input checked="" type="checkbox"/> ZW Zimbabwe |
| <input type="checkbox"/> KP Democratic People's Republic of Korea | |
| <input checked="" type="checkbox"/> KR Republic of Korea | |
| <input checked="" type="checkbox"/> KZ Kazakhstan | |

Check-boxes reserved for designating States which have become party to the PCT after issuance of this sheet:

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)

Box No. VI PRIORITY CLAIM <input type="checkbox"/> Further priority claims are indicated in the Supplemental Box.				
Filing date of earlier application (day/month/year)	Number of earlier application	national application: country	regional application:* regional Office	international application: receiving Office
item (1) 25 February 2000 (25.02.00)	60/185,220	US		
item (2)				
item (3)				

☒ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office) identified above as item(s): (1)

* Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.

Box No. VII INTERNATIONAL SEARCHING AUTHORITY		
Choice of International Searching Authority (ISA) (if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):	Request to use results of earlier search; reference to that search (if an earlier search has been carried out by or requested from the International Searching Authority):	
ISA / EP	Date (day/month/year)	Number Country (or regional Office)

Box No. VIII CHECK LIST; LANGUAGE OF FILING	
This international application contains the following number of sheets:	This international application is accompanied by the item(s) marked below:
request : 5	1. <input checked="" type="checkbox"/> fee calculation sheet
description (excluding sequence listing part) : 23	2. <input type="checkbox"/> separate signed power of attorney
claims : 12	3. <input type="checkbox"/> copy of general power of attorney; reference number, if any:
abstract : 2	4. <input type="checkbox"/> statement explaining lack of signature
drawings : 0	5. <input type="checkbox"/> priority document(s) identified in Box No. VI as item(s):
sequence listing part of description : _____	6. <input type="checkbox"/> translation of international application into (language):
Total number of sheets : 42	7. <input type="checkbox"/> separate indications concerning deposited microorganisms or other biological material
	8. <input type="checkbox"/> nucleotide and/or amino acid sequence listing in computer readable form
	9. <input checked="" type="checkbox"/> other (specify): cover letter to USRO; Return Postcard

Figure of the drawings which should accompany the abstract:	Language of filing of the international application: English
---	---

Box No. IX SIGNATURE OF APPLICANT OR AGENT
<p align="center">MA, Dangshe, et al</p> <p align="center">By: <u><i>Dragan J. Karadzic</i></u></p> <p align="center">Dragan J. Karadzic</p>

1. Date of actual receipt of the purported international application: JC03 Rec'd PCT/PTO 23 FEB 2001	2. Drawings: <input type="checkbox"/> received: <input type="checkbox"/> not received:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:	
4. Date of timely receipt of the required corrections under PCT Article 11(2):	
5. International Searching Authority (if two or more are competent): EP	
6. <input type="checkbox"/> Transmittal of search copy delayed until search fee is paid.	

Date of receipt of the record copy by the International Bureau:

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/05927

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K51/04 A61K51/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data, EMBASE, BIOSIS, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 428 154 A (MAEGERSTAEDT MICHAEL A ET AL) 27 June 1995 (1995-06-27) claims	1
X	WO 99 30745 A (GOVINDAN SERENGULAM V ;HANSEN HANS (US); GRIFFITHS GARY L (US); IM) 24 June 1999 (1999-06-24) claims	1-20

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

25 March 2002

Date of mailing of the international search report

17/04/2002

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Berte, M

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 01/05927

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE CA 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; SCHEINBERG, DAVID A. ET AL: "Clinical application of targeted alpha particles for cancer therapy" retrieved from STN Database accession no. 1998:141327 XP002194098 abstract & BOOK OF ABSTRACTS, 215TH ACS NATIONAL MEETING, DALLAS, MARCH 29-APRIL 2 (1998), NUCL-087 PUBLISHER: AMERICAN CHEMICAL SOCIETY, WASHINGTON, D. C.,</p>	1-20
P, X	<p>WO 00 59896 A (US HEALTH ;DEAL KIM (US); BRECHBIEL MARTIN W (US)) 12 October 2000 (2000-10-12) claims</p>	1
P, X	<p>MCDEVITT, M. R. (1) ET AL: "A novel alpha particle emitting 225Ac labeled anti-CD33 antibody construct: Synthesis and in vitro evaluation of biochemistry, potency, specificity and mechanism of cell death." JOURNAL OF NUCLEAR MEDICINE, (MAY, 2000) VOL. 41, NO. 5 SUPPL., PP. 30P. PRINT. MEETING INFO.: 47TH ANNUAL MEETING OF THE SOCIETY OF NUCLEAR MEDICINE ST. LOUIS, MISSOURI, USA JUNE 03-07, 2000 SOCIETY OF NUCLEAR MEDICINE., XP002194097 No116 page 30P</p>	1
E	<p>WO 02 05859 A (COCKBAIN JULIAN ;LARSEN ROY H (NO); ANTICANCER THERAPEUTIC INV S A) 24 January 2002 (2002-01-24) claims</p>	1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/05927

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5428154	A	27-06-1995	AT 134999 T	15-03-1996
			AU 655704 B2	05-01-1995
			AU 3210893 A	01-04-1993
			AU 630362 B2	29-10-1992
			AU 3842889 A	12-12-1989
			CA 1339015 A1	25-03-1997
			DE 68925904 D1	11-04-1996
			DE 68925904 T2	31-10-1996
			EP 0416033 A1	13-03-1991
			IL 90409 A	12-09-1996
			IL 113068 A	14-11-1996
			JP 2582341 B2	19-02-1997
			JP 7258281 A	09-10-1995
			JP 7020989 B	08-03-1995
			JP 3503531 T	08-08-1991
			WO 8911475 A1	30-11-1989
WO 9930745	A	24-06-1999	US 6120768 A	19-09-2000
			AU 1825899 A	05-07-1999
			WO 9930745 A2	24-06-1999
WO 0059896	A	12-10-2000	AU 4450100 A	23-10-2000
			WO 0059896 A1	12-10-2000
WO 0205859	A	24-01-2002	NO 20003457 A	07-01-2002
			WO 0205859 A2	24-01-2002